

产品名称: **S3I-201**
 产品别名: **NSC 74859**

生物活性:																														
Description	NSC 74859 is a selective Stat3 inhibitor with an IC ₅₀ of 86 μM.																													
IC₅₀ & Target [1]	STAT3																													
	86 μM (IC ₅₀)																													
In Vitro	<p>NSC 74859 (S3I-201) preferentially inhibits Stat3 DNA-binding activity over that of Stat1 (IC₅₀ values, Stat3•Stat3, 86±33 μM; Stat1•Stat3, 160±43 μM; and Stat1•Stat1, >300 μM) and inhibits that of Stat5 with IC₅₀ of 166±17 μM). NSC 74859 significantly reduces viable cell numbers and inhibits growth of transformed mouse fibroblasts NIH 3T3/v-Src and breast carcinoma cell lines (MDA-MB-231, MDA-MB-435, and MDA-MB-468). At 30-100 μM, NSC 74859 induces significant apoptosis in the representative human breast carcinoma cell line MDA-MB-435 and NIH 3T3/v-Src, both of which harbor constitutively active Stat3. The breast carcinoma MDA-MB-435 cell line is more sensitive to 30 μM NSC 74859. By contrast, the human breast cancer MDA-MB-453 cells and the normal mouse fibroblasts (NIH 3T3), which do not contain abnormal Stat3 activity, are less sensitive to NSC 74859 at 100 μM or less. At 300 μM or higher, NSC 74859 induced general, nonspecific cytotoxicity independent of Stat3 activation status[1]. Huh-7 cells do not express β2SP or TBGFR2 and are sensitive to STAT3 inhibition, with an IC₅₀ of 100 μM for NSC 74859, regardless of CD133⁺ status. The IC₅₀ of NSC 74859 is 150 μM for Huh-7 and SNU-398 cells, 15 μM for SNU-475 cells and 200 μM for SNU-182 cells. NSC 74859 inhibits breast carcinoma MDA-MB-435, MDA-MB-453 and MDA-MB-231 cell lines with an IC₅₀ close to 100 μM[2].</p>																													
In Vivo	<p>Human breast (MDA-MB-231) tumor-bearing mice are given an i.v. injection of NSC 74859 (S3I-201) or vehicle every 2 or every 3 days for 2 weeks, and tumor measurements are taken every 2-3 days. Compared with control (vehicle-treated) tumors, which continued to grow, human breast tumors in mice that received S3I-201 display strong growth inhibition. Continued evaluation of treated mice on termination of treatment shows no resumption of tumor growth, suggesting potentially a long-lasting effect of S3I-201 on tumor growth[1]. Compared with vehicle-treated control tumors (n=15), which continued to grow, S3I-201 treatment of somatotroph tumor xenografts (n=15) significantly attenuated tumor growth for the duration of the experiment. Tumors derived from NSC 74859-treated rats are significantly smaller than those from the untreated group (220±16 mm³ vs. 287±16 mm³, P<0.01) as early as 5 days after NSC 74859 injection. Fifteen days after treatments, the average tumor volume of NSC 74859-treated rats is 64% of that of controls (449±40 mm³ vs. 708±83 mm³, P<0.01). Rats are sacrificed and tumors are harvested 15 days after treatment initiation. The average tumor weight of NSC 74859-treated rats is 78±8 mg, while tumors derived from control rats weighed 114±13 mg (32% reduction; P<0.05)[3].</p>																													
<p>In Vitro: DMSO : 100 mg/mL (273.70 mM; Need ultrasonic)</p> <table border="1"> <thead> <tr> <th rowspan="2">Preparing Stock Solutions</th> <th>Solvent</th> <th>Mass</th> <th rowspan="2">1 mg</th> <th rowspan="2">5 mg</th> <th rowspan="2">10 mg</th> </tr> <tr> <th colspan="2">Concentration</th> </tr> </thead> <tbody> <tr> <td></td> <td></td> <td>1 mM</td> <td>2.7370 mL</td> <td>13.6851 mL</td> <td>27.3703 mL</td> </tr> <tr> <td></td> <td></td> <td>5 mM</td> <td>0.5474 mL</td> <td>2.7370 mL</td> <td>5.4741 mL</td> </tr> <tr> <td></td> <td></td> <td>10 mM</td> <td>0.2737 mL</td> <td>1.3685 mL</td> <td>2.7370 mL</td> </tr> </tbody> </table> <p>*请根据产品在不同溶剂中的溶解度, 选择合适的溶剂配制储备液, 该产品在溶液状态不稳定, 建议您现用现配, 即刻使用。</p>					Preparing Stock Solutions	Solvent	Mass	1 mg	5 mg	10 mg	Concentration				1 mM	2.7370 mL	13.6851 mL	27.3703 mL			5 mM	0.5474 mL	2.7370 mL	5.4741 mL			10 mM	0.2737 mL	1.3685 mL	2.7370 mL
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<p>Solvent&Solubility</p>	<p>In Vivo:</p> <p>请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：</p> <p>——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用；以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶</p> <p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 7.5 mg/mL (20.53 mM); Clear solution</p> <p>此方案可获得 ≥ 7.5 mg/mL (20.53 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 μL 75.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。</p> <p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 7.5 mg/mL (20.53 mM); Clear solution</p> <p>此方案可获得 ≥ 7.5 mg/mL (20.53 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 μL 75.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 7.5 mg/mL (20.53 mM); Clear solution</p> <p>此方案可获得 ≥ 7.5 mg/mL (20.53 mM, 饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。</p> <p>以 1 mL 工作液为例，取 100 μL 75.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p>
<p>References</p>	<p>[1]. Siddiquee K, et al. Selective chemical probe inhibitor of Stat3, identified through structure-based virtual screening, induces antitumor activity. Proc Natl Acad Sci U S A. 2007 May 1;104(18):7391-6.</p> <p>[2]. Lin L, et al. The STAT3 inhibitor NSC 74859 is effective in hepatocellular cancers with disrupted TGF-β signaling. Oncogene. 2009 Feb 19;28(7):961-72.</p> <p>[3]. Zhou C, et al. STAT3 upregulation in pituitary somatotroph adenomas induces hypersecretion. J Clin Invest. 2015 Apr;125(4):1692-702</p>
<p>实验参考:</p>	
<p>Cell Assay</p>	<p>Proliferating cells are treated with or without NSC 74859 (30-100 μM) for up to 48 h. In some cases, cells are first transfected with Stat3C, ST3-NT, or ST3-SH2 domain or mock-transfected for 24 h before treatment with compound for an additional 24-48 h. Cells are then detached and analyzed by annexin V binding and flow cytometry to quantify the percent apoptosis[1].</p>
<p>Animal Administration</p>	<p>Mice[1] Six-week-old female athymic nude mice are used. Athymic nude mice are injected in the left flank area s.c. with 5×10⁶ human breast cancer MDA-MB-231 cells in 100 μL of PBS. After 5-10 days, tumors with a diameter of 3 mm are established. Animals are given NSC 74859 i.v. at 5 mg/kg every 2 or 3 days for 2 weeks and monitored every 2 or 3 days. Animals are stratified so that the mean tumor sizes in all treatment are nearly identical. Tumor volume is calculated according to the formula $V=0.52 \times a^2 \times b$, where a is the smallest superficial diameter and b is the largest superficial diameter.</p> <p>Rats[3] Four-week-old female Wistar Furth rats are used. GH3 cells (5×10⁵ cells in 100 μL Matrigel) are</p>

	<p>subcutaneously injected into the left lumbar area. After 7 days, tumors with a volume of approximately 100 mm³ are established. Rats are given NSC 74859 intravenously at 5 mg/kg every 2 or 3 days for 2 weeks. Tumor size is measured by caliper measurements twice a week, and volume is calculated as follows: $\text{volume}=(\text{length}\times\text{width}^2)/2$. Three weeks after cell inoculations, animals are euthanized and excised tumors are weighed. Blood samples are collected 1 day before S3I-201 treatment and again on the day of euthanization. Serum GH and prolactin are assessed by RIA or ELISA, respectively.</p>
References	<p>[1]. Siddiquee K, et al. Selective chemical probe inhibitor of Stat3, identified through structure-based virtual screening, induces antitumor activity. Proc Natl Acad Sci U S A. 2007 May 1;104(18):7391-6.</p> <p>[2]. Lin L, et al. The STAT3 inhibitor NSC 74859 is effective in hepatocellular cancers with disrupted TGF-β signaling. Oncogene. 2009 Feb 19;28(7):961-72.</p> <p>[3]. Zhou C, et al. STAT3 upregulation in pituitary somatotroph adenomas induces hypersecretion. J Clin Invest. 2015 Apr;125(4):1692-702</p>



源叶生物